

Amendments to the Claims:

This listing of claims will replace all prior versions, and listings, of claims in the application:

Listing of Claims:

Claim 1 (currently amended): An isolated nucleic acid ~~that encodes a guanine nucleotide exchange factor for the small GTPase Ral and a downstream effector for both Rit and Ras, or a protein with RasGEFN domain, RasGEF domain, and/or RA domain,~~
comprising:

- (a) a nucleotide sequence selected from the group consisting of:
 - (i) SEQ ID NO: 1;
 - (ii) the complete complement of the sequences set forth in (i);
 - (iii) the nucleotide sequence of SEQ ID NO: 2;
 - (iv) a degenerate variant of the sequences set forth in (iii); and
 - (v) the complete complement of the sequences set forth in (iii) and (iv); or
- (b) a nucleotide sequence selected from the group consisting of:
 - (i) a nucleotide sequence that encodes a polypeptide having the sequence of
SEQ ID No: 3;

- (ii) a nucleotide sequence that encodes a polypeptide ~~having the at least 90%~~
identical in sequence to SEQ ID NO: 3, ~~with conservative amino acid~~
~~substitutions~~; and
- (iii) a nucleotide sequence that is the complete complement of the nucleotide
sequences set forth in of any of (i) and (ii),

wherein said isolated nucleic acid encodes a guanine nucleotide exchange factor for the
small GTPase Ral and a downstream effector for both Rit and Ras, or a protein with
RasGEFN domain, RasGEF domain, or RA domain and wherein said isolated nucleic
acid comprising a nucleotide sequence selected from group (b) is no more than about 100
kb in length.

Claim 2 (currently amended): The isolated nucleic acid of claim 1 wherein said nucleic
acid, or the complete complement of said nucleic acid, encodes a polypeptide having
guanine nucleotide exchange activity for the small GTPase Ral, and being a downstream
effector for both Rit and Ras.

Claim 3 (original): The isolated nucleic acid of claim 1, wherein said nucleic acid, or the
complement of said nucleic acid, is expressed in adrenal, adult liver, bone marrow, brain,
fetal liver, heart, kidney, lung, placenta, colon, skeletal muscle and prostate, as well as a
cell line, HeLa.

Claim 4 (currently amended): A nucleic acid probe, comprising:

~~(a) — the nucleic acid of claim 1; or~~

~~(b) — at least 17 contiguous nucleotides of SEQ ID NO: 4,~~

~~wherein said probe according to (b) is no longer than about 100 kb in length.~~

Claim 5 (original): The probe of claim 4, wherein said probe is detectably labeled.

Claim 6 (original): The probe of claim 4, attached to a substrate.

Claim 7 (withdrawn): A microarray, wherein at least one probe of said array is a probe according to claim 4.

Claim 8 (original): The isolated nucleic acid molecule of claim 1, wherein said nucleic acid molecule is operably linked to one or more expression control elements.

Claim 9 (original): A replicable vector comprising a nucleic acid molecule of claim 1.

Claim 10 (original): A replicable vector comprising an isolated nucleic acid molecule of claim 8.

Claim 11 (original): A host cell transformed to contain the nucleic acid molecule of any one of claims 1 or 8 - 10, or the progeny thereof.

Claim 12 (withdrawn): A method for producing a polypeptide, the method comprising: culturing the host cell of claim 11 under conditions in which the protein encoded by said nucleic acid molecule is expressed.

Claim 13 (withdrawn): An isolated polypeptide produced by the method of claim 12.

Claim 14 (withdrawn): An isolated polypeptide, comprising:

- (a) an amino acid sequence of SEQ ID NO: 3;
- (b) an amino acid sequence having at least 65% amino acid sequence identity to that of (a);
- (c) an amino acid sequence according to (a) in which at least 95% of deviations from the sequence of (a) are conservative substitutions; or
- (d) a fragment of at least 8 contiguous amino acids of any of (a) – (c).

Claim 15 (withdrawn): A fusion protein, said fusion protein comprising a polypeptide of claim 14 fused to a heterologous amino acid sequence.

Claim 16 (withdrawn): The fusion protein of claim 15, wherein said heterologous amino acid sequence is a detectable moiety.

Claim 17 (withdrawn): The fusion protein of claim 16, wherein said detectable moiety is fluorescent.

Claim 18 (withdrawn): The fusion protein of claim 15, wherein said heterologous amino acid sequence is an Ig Fc region.

Claim 19 (withdrawn): An isolated antibody, or antigen-binding fragment or derivative thereof, the binding of which can be competitively inhibited by a polypeptide of claim 14.

Claim 20 (withdrawn): A transgenic non-human animal modified to contain the nucleic acid molecule of any one of claims 1 or 8 – 10.

Claim 21 (withdrawn): A transgenic non-human animal unable to express the endogenous orthologue of the nucleic acid molecule of claim 1.

Claim 22 (withdrawn): A method of identifying agents that modulate the expression of RGL3, the method comprising:

contacting a cell or tissue sample believed to express RGL3 with a chemical or biological agent, and then
comparing the amount of RGL3 expression in said cell or tissue sample with that of a control,
changes in the amount relative to control identifying an agent that modulates expression of RGL3.

Claim 23 (withdrawn): A method of identifying agonists and antagonists of RGL3, the method comprising:

contacting a cell or tissue sample believed to express RGL3 with a chemical or biological agent, and then
comparing the activity of RGL3 with that of a control,
increased activity relative to a control identifying an agonist, decreased activity relative to a control identifying an antagonist.

Claim 24 (withdrawn): A purified agonist of the polypeptide of claim 14.

Claim 25 (withdrawn): A purified antagonist of the polypeptide of claim 14.

Claim 26 (withdrawn): A method of identifying a specific binding partner for a polypeptide according to claim 14, the method comprising:

contacting said polypeptide to a potential binding partner; and
determining if the potential binding partner binds to said polypeptide.

Claim 27 (withdrawn): The method of claim 26, wherein said contacting is performed *in vivo*.

Claim 28 (withdrawn): A purified binding partner of the polypeptide of claim 14.

Claim 29 (withdrawn): A method for detecting a target nucleic acid in a sample, said target being a nucleic acid according to claim 1, the method comprising:

- (a) hybridizing the sample with a probe comprising at least 17 contiguous nucleotides of a sequence complementary to said target nucleic acid in said sample under high stringency hybridization conditions, and
- (b) detecting the presence or absence, and optionally the amount, of said binding.

Claim 30 (withdrawn): A method of diagnosing a disease caused by mutation in RGL3, comprising:

detecting said mutation in a sample of nucleic acids that derives from a subject suspected to have said disease.

Claim 31 (withdrawn): A method of diagnosing or monitoring a disease caused by altered expression of RGL3, comprising:
determining the level of expression of RGL3 in a sample of nucleic acids or proteins that derives from a subject suspected to have said disease,
alterations from a normal level of expression providing diagnostic and/or monitoring information.

Claim 32 (original): A diagnostic composition comprising the nucleic acid of claim 1, said nucleic acid being detectably labeled.

Claim 33 (original): The diagnostic composition of claim 32, wherein said composition is further suitable for *in vivo* administration.

Claim 34 (withdrawn): A diagnostic composition comprising the polypeptide of claim 14, said polypeptide being detectably labeled.

Claim 35 (withdrawn): The diagnostic composition of claim 34, wherein said composition is further suitable for *in vivo* administration.

Claim 36 (withdrawn): A diagnostic composition comprising the antibody, or antigen-binding fragment or derivative thereof, of claim 19.

Claim 37 (withdrawn): The diagnostic composition of claim 36, wherein said antibody or antigen-binding fragment or derivative thereof is detectably labeled.

Claim 38 (withdrawn): The diagnostic composition of claim 37, wherein said composition is further suitable for *in vivo* administration.

Claim 39 (original): A pharmaceutical composition comprising the nucleic acid of claim 1 and a pharmaceutically acceptable excipient.

Claim 40 (withdrawn): A pharmaceutical composition comprising the polypeptide of claim 14 and a pharmaceutically acceptable excipient.

Claim 41 (withdrawn): A pharmaceutical composition comprising the antibody or antigen-binding fragment or derivative thereof of claim 19 and a pharmaceutically acceptable excipient.

Claim 42 (withdrawn): A pharmaceutical composition comprising the agonist of claim 24 and a pharmaceutically acceptable excipient.

Claim 43 (withdrawn): A pharmaceutical composition comprising the antagonist of claim 25 and a pharmaceutically acceptable excipient.

Claim 44 (withdrawn): A method for treating or preventing a disorder associated with decreased expression or activity of RGL3, the method comprising administering to a subject in need of such treatment an effective amount of the pharmaceutical composition of any of claims 39, 40 or 42.

Claim 45 (withdrawn): A method for treating or preventing a disorder associated with increased expression or activity of RGL3, the method comprising administering to a subject in need of such treatment an effective amount of the pharmaceutical composition of claim 41 or 43.

Claim 46 (withdrawn): A method of modulating the expression of a nucleic acid according to claim 1, the method comprising:
administering an effective amount of an agent which modulates the expression of a nucleic acid according to claim 1.

Claim 47 (withdrawn): A method of modulating at least one activity of a polypeptide according to claim 14, the method comprising:

administering an effective amount of an agent which modulates at least one activity of a polypeptide according to claim 14.

Claim 48 (new): An isolated nucleic acid, comprising: a nucleotide sequence selected from the group consisting of:

- (i) a nucleotide sequence that encodes a polypeptide at least 95% identical in sequence to SEQ ID NO: 3; and
- (ii) a nucleotide sequence that is the complete complement of the nucleotide sequences of (i),

wherein said isolated nucleic acid encodes a guanine nucleotide exchange factor for the small GTPase Ral and a downstream effector for both Rit and Ras, or a protein with RasGEFN domain, RasGEF domain, or RA domain.

Claim 49 (new): An isolated nucleic acid, comprising: a nucleotide sequence selected from the group consisting of:

- (i) a nucleotide sequence that encodes a polypeptide at least 99% identical in sequence to SEQ ID NO: 3; and
- (ii) a nucleotide sequence that is the complete complement of the nucleotide sequences of (i),

wherein said isolated nucleic acid encodes a guanine nucleotide exchange factor for the small GTPase Ral and a downstream effector for both Rit and Ras, or a protein with RasGEFN domain, RasGEF domain, or RA domain.